

- USSN 08/896,933 "Tumor Killing Effects of Enterotoxins and Related Compounds," filed 18 July 1997.
- USSN 60/085,506, "Compositions and Methods for Treatment of Cancer," filed 05 May
 1998.
- USSN 60/094,952 "Compositions and Methods for Treatment of Cancer" filed 31 July 1998.
- 9. USSN 60/033,172 "Superantigen-Based Methods and Compositions for Treatment of Cancer," filed 17 December1996.
- 10. USSN 60/044,074 "Superantigen-Based Methods and Compositions for Treatment of Cancer," filed 17 April 1997.
- USSN 09/061,334 "Tumor Cells with Increased Immunogenicity and Uses Thereof," filed 17 April 1998.
- USSN 09/311,581 "Compositions and Methods for Treating Neoplastic Disease," filed 14 May 1999.
- 12. USSN 09/650.884 "Compositions and Methods for Treating Neoplastic Disease," filed 30 August 2000.

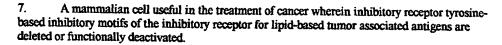
Moreover, all references cited herein are incorporated by reference, whether specifically incorporated or not.

Having now fully described this invention, it will be appreciated by those skilled in the art that the same can be performed within a wide range of equivalent parameters, concentrations, and conditions without departing from the spirit and scope of the invention and without undue experimentation.

While this invention has been described in connection with specific embodiments thereof, it will be understood that it is capable of further modifications. This application is intended to cover any variations, uses, or adaptations of the invention following, in general, the principles of the invention and including such departures from the present disclosure as come within known or customary practice within the art to which the invention pertains and as may be applied to the essential features hereinbefore set forth as follows in the scope of the appended claims.

WHAT IS CLAIMED IS:

- A receptor in a mammalian cell useful in the treatment of cancer which inhibits cellular activation by receptors specific for lipid-based tumor associatiated antigens.
- 2 The receptor of claim 1 wherein the lipid antigen is a bacterial, fungal, protozoal or mycobacterial antigen.
- 3. The inhibitory receptor of claims 1 and 2 wherein said inhibitory receptor contains an inhibitory receptor tyrosine-based inhibitory motifs (ITIMs).
- 4. The inhibitory receptor of claim 1, 2 wherein said receptor is specific for lipid-based tumor associated antigen and/or self MHC or CD1 molecules.
- A receptor in a mammalian cell wherein said receptor inhibits cellular activation by receptors specific for lipid-based infectious disease associated antigens derived from bacteria, fungi, mycobacterium, parasite, virus, eukaryote or prokaryote antigens in the context of MHC or CD1.
- 6. A mammalian cell useful in the treatment of cancer wherein the inhibitory receptor for lipid-based tumor associated antigens is deleted or functionally deactivated.



- 8. A mammalian cell useful in the treatment of cancer wherein the the inhibitory receptor for superantigens associated with self antigens are functionally deleted.
- A mammalian cell useful in the treatment of cancer wherein the inhibitory receptor for tumor associated lipid antigens and superantigens are deleted or functionally deactivated.
- 10. The lipid-based tumor associated antigens of claims 1, 2, 4, 6, 9, wherein said lipid-based tumor associated antigen is selected from the group consisting of glycolipids, proteolipids, glycosphingolipids, sphingolipids, gangliosides, phytoglycolipids.
- 11. The lipid antigens derived from bacteria, mycobacteria, fungi and protozoa marine invertebrates of claim 2 wherein said lipid antigens are selected from the group consisting of glycosylceramides, glycolipids, proteolipids, glycosphingolipids, gangliosides and sphingolipids with inositolphosphate-containing head groups, phytoglycolipids, mycoglycolipids, lipoarabinan and mycolic acid.
- The sphingolipid antigens of claim 11 wherein the sphingolipid contains inositolphosphate-containing head groups with the general structure of ceramide-P-myoinositol-X with X referring to polar substituents consisting of ceramide-p-inositol-mannose, inositol-1-P-(6)mannose(a1,2inositol-1P-(1)ceramide, (inositol-P)2-ceramide, inositol-P-inositol-P-ceramide, inositol-P-ceramide.
- 13. The mammalian cell of claim 6-9 wherein said cell is an immunocyte selected from a group consisting of T cell, NK cell, NKT cells
- 14. A mammalian cell of claim 7 wherein the superantigen is selected from a group consisting of a staphylococcal enterotoxin, a streptococcal pyrogenic exotoxin, mycoplasma arthitides, rabies antigen, clostridial product.
- 15. A mammalian cell useful in the treatment of cancer wherein the inhibitory receptor for glycan-based tumor associated antigens is deleted or functionally deactivated.
- 16. The glycan antigens of claim 15 wherein said glycan antigen is selected from the group consisting of peptidoglycans or glycan phosphotidylinositol (GPI) structures.
- 17. A mammalian cell useful in the treatment of cancer wherein the the inhibitory receptor for superantigen-associated self antigens are functionally deleted or inactivated.
- 18. The self antigens of claims 17 wherein said self antigens consist of a MHC or CD1 molecule.
- 19. A mammalian cell useful in the treatment of cancer wherein the inhibitory receptors and/or immune receptor tyrosine based inhibitory motifs which inhibits cellular activation by receptors specific for lipid-based tumor associated antigens and superantigens are deleted or functionally deactivated.
- 20. The superantigen of claims 17 wherein said superantigen is selected from a group consisting of the staphylococcal enterotoxins SEA, SEB, SEC, SEC1, SEC2, SEC3, SED, SEE, TSST-1 or streptococcal pyrogenic exotoxins, mycoplasma arthritides, rabies virus, mammary



- 21. A mammalian cell in which the inhibitory receptor for lipid-based infectious disease associated antigens and/or immune receptor tyrosine based inhibitory motifs which inhibits cellular activation by receptors specific for lipid-based infectious disease associated antigens derived from bacteria, fungi, mycobacteria, parasite, virus, eukaryote or prokaryote antigens are deleted or functionally deactivated.
- 22. The mammalian cell of claims 13, 14, 15, 17, 18, 21 wherein said cell is an immunocyte selected from a group consisting of T cells, NK cells, NKT cells
- 23. The lipid antigens of claims 21 wherein said lipid-based infectious disease associated antigen or fatty acid is mycolic acid or lipoarabinan,
- A method of treating cancer in a mammal, said method comprising inactivating or deleting inhibitory receptors or immune receptor tyrosine based inhibitory motifs in immunocytes which inhibit activating receptors specific for lipid-based tumor associated lipid antigens or superantigens.
- 25. A method of inactivation or deletion of receptors or ITIMs in immunocytes which inhibit cell activating receptors specific for lipid-based tumor associated antigens and superantigens comprising inactivation or deletion of nucleic acids encoding ITIMs.
- 26. A method for producing a tumoricidal immunocyte population in vivo said method comprising allowing a tumor associated lipid antigen and superantigen to contact immunocyte activation receptors specific for tumor associated lipid antigens and superantigens in which inhibitory receptors or ITIMs which inhibit said cell activation by receptors specific for lipid-based tumor associated antigens are inactivated or deleted.
- 27. A method for producing a tumoricical immunocyte population *ex vivo*, said method comprising:
- a) allowing a lipid-based tumor associated antigen and superantigen to contact immunocyte activation receptors specific for lipid-based tumor associated antigens and superantigens in which inhibitory receptors or ITIMs which inhibit said cell activating receptors for lipid-based tumor associated antigens are deleted or inactivated.
- b) administering said tumoricidally activated immunocytes to the host.
- 28. A method of producing a immunocyte population effective against infectious disease in a mammal *in vivo* said method comprising:
- a) allowing a lipid-based infectious disaease associated antigen and superantigen to contact immunocyte activation receptors specific for and superantigens in which inhibitory receptors or ITIMs which inhibit said cell activation receptors specific for lipid-based infectious disaease associated antigen and superantigens are inactivated or deleted.
- 29. A method for producing an immunocyte population effective against infectious disease in a mammal ex vivo, said method comprising:





- a) allowing a lipid-based infectious disease associated antigen and superantigen to contact immunocyte activation receptors specific for lipid-based infectious disease associated antigens and superantigens in which inhibitory receptors or inhibitory receptors with tyrosine-based inhibitory motifs which inhibit said cell activating receptors for lipid-based infectious disease associated antigens are deleted or inactivated.
- b) administering said immunocyte population effective against infectious disease to the host.
- 30. The immunocytes of claims 26-29 wherein the said immunocytes comprise a group consisting of a T cell, NK cell or NKT cell
- 31. The immunocytes of claim 27, 29 wherein the said immunocytes are expanded in cytokines ex vivo prior to said administration
- 32. The method of claims 24-29 wherein said superantigen comprises a staphylococcal enterotoxin, a streptococcal pyrogenic exotoxin, mycoplasma arthritites, rabies virus, clostridial antigen, heat shock protein.
- 33. The staphylococcal enterotoxin of claim 32, wherein said enterotoxin is selected from the group consisting of SEA, SEB, SEC1, SEC2, SED, SEE, SEF, TSST-1, SPEA, SPEB, SPEC, Streptococcal pyogenic exotoxin.
- 34. The superantigen of any of the claims wherein said superantigen is expressed by a tumor cell or accessory cell which has been transfected with a nucleic acid encoding a superantigen.
- 35. The superantigen of claims 34 wherein said superantigen is expressed on the surface of a cell.
- 36. The cell of claim 35 wherein said cell is a tumor cell or an accessory cell.
- 37. The superantigen transfected tumor cell or accessory cell of claims 34-36 comprising transfecting said transfected cell with additional nucleic acids selected from a group comprising an adhesion molecule, an MHC molecule, a costimulatory molecule or a plurality thereof wherein said transfected cell expresses said encoded molecule(s) from said nucleic acid.
- 38. The transfected tumor cell or accessory cell of claims 34-37 wherein said transfected cell is transfected in vivo.
- 39. The transfected tumor cell or accessory cell of claims 34-37 wherein said transfected cell is transfected ex vivo...
- 40. A mammalian cell wherein inhibitory receptors or their ITIMs and Fas ligand receptors are deleted or functionally inactivated
- 41. The mammalian cell of claim 30, 31 wherein said cell is an immunocyte selected from a group consisting of T cell, NKT cells
- 42. A method of treating cancer by wherein lipid-based tumor associated antigen or superantigen agonist motifs selectively contact immunocyte activating receptors and not immunocyte inhibitory receptors in vivo thereby producing an immunocyte population which is